

WHAT IS CLAIMED IS:

1. A method of cellular analysis, comprising introducing one or more heterologous cells into a fish; and
5 analyzing a property of the cells or the fish.

2. The method of claim 1, wherein the fish is a zebrafish, medaka, Giant rorio or puffer fish.

10 3. The method of claim 1, wherein the heterologous cells remain viable at least until the analyzing step.

4. The method of claim 1, further comprising culturing the fish whereby the heterologous cells proliferate in the fish.

15 5. The method of claim 1, wherein the property is an mRNA expression profile of the cells or the fish.

6. The method of claim 1, wherein the analyzing comprises testing for
20 presence of a set of differentiation markers in the heterologous cells or the fish.

7. The method of claim 1, further comprising contacting the fish with an agent, and wherein the analyzing determines whether the property is responsive to administration of the agent.

25 8. The method of claim 7, wherein the agent is a growth factor, a hormone, a cytokine, a natural product, or a member of a combinatorial library.

9. The method of claim 7, wherein the agent is cytotoxic.

30 10. The method of claim 7, wherein the property is a differentiation marker, survival of the fish, proliferation of the heterologous cells, movement of the

heterologous cells relative to an initial site of introduction, death of heterologous cells or cells of the fish, or proliferation of the heterologous cells.

11. The method of claim 7, wherein the property is proliferation of the
5 heterologous cells.

12. The method of claim 7, wherein the property is a teratogenic response of the fish to the introduction of heterologous cells.

10 13. The method of claim 7, wherein the property is expression of a protein within the heterologous cells.

14. The method of claim 7, wherein the property is secretion of a protein from the heterologous cells.

15 15. The method of claim 1, wherein the cells are stem cells.

16. The method of claim 1, wherein the cells are pluripotent or mesenychmal stem cells.

20 17. The method of claim 1, wherein the cells are differentiated cells.

18. The method of claim 1, wherein the cells are myocytes.

25 19. The method of claim 1, wherein the cells are chondrocytes.

20. The method of claim 1, wherein the cells are pancreatic, renal, hepatic cells, glial cells, endothelial cells or epidermal cells.

30 21. The method of claim 1 , wherein the heterologous cells are human cells.

22. The method of claim 1, further comprising recovering the heterologous cells from the fish.

23. The method of claim 22, wherein the heterologous cells are recovered after proliferation in the fish.

24. The method of claim 1, wherein the heterologous cells are from a patient biopsy, the property is proliferation or metastasis of the cells, and the analyzing indicates prognosis of the patient.

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25. The method of claim 1, wherein the heterologous cells are bacterial cells.

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26. The method of claim 1, further comprising infecting the heterologous cells with a virus before or after introducing the cells into the fish.

27. The method of claim 26, wherein the virus infects the heterologous cells without infecting cells of the fish.

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28. The method of claim 7, wherein the cells are cancer cells.

29. The method of claim 28, wherein the analyzing comprising monitoring an effect of the agent on the cancerous cells.

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30. The method of claim 28, wherein the cancerous cells are human cells.

31. The method of claim 28, wherein the cancerous cells are from a human cell line.

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32. The method of claim 28, wherein the cancerous cells are from a human tumor.

33. The method of claim 28, wherein the cancerous cells are selected from the group consisting of leukemias, sarcomas, blastomas, teratomas, gliomas, neurofibromatomas, and carcinomas.

5 34. The method of claim 1, wherein the introducing step comprises microinjecting the heterologous cells into an embryonic form of the fish.

35. The method of claim 34, wherein the introducing step comprises microinjecting the heterologous cells into an embryonic form of the fish.

10 36. The method of claim 35, wherein the cells are microinjected into the body of the embryo.

15 37. The method of claim 35, wherein the cells are microinjected into the yolk of the embryo.

38. The method of claim 7, wherein the agent is introduced into media containing the fish or is introduced by injection into the fish.

20 39. The method of claim 28, wherein the heterologous cells are introduced before the agent is administered.

40. The method of claim 28, wherein the heterologous cells proliferate in the fish before the agent is administered.

25 41. The method of claim 28, wherein the heterologous cells metastasize in the fish before the agent is administered.

42. The method of claim 28, wherein the agent is administered before 30 the cancerous cells are introduced.

43. The method of claim 28, wherein the effect of the agent is an inhibition of proliferation of the cancerous cells relative to the proliferation in a control fish in which the cancerous cells have been introduced without the agent.

5 44. The method of claim 28, wherein the effect of the agent is an inhibition of metastasis of the cancerous cells relative to the metastasis that occurs in a control fish in which the cancerous cells have been introduced without the agent.

10 45. The method of claim 28, further comprising performing an assay to determine whether the agent has activity against cells in the fish.

46. The method of claim 45, wherein the assay comprises monitoring development of one or more organs in a fish embryo.

15 47. The method of claim 45, wherein the monitoring comprises detecting a morphological defect in a fish embryo.

48. The method of claim 45, wherein the assay comprises detecting necrotic cells in the fish embryo.

20 49. The method of claim 45, wherein the assay comprises performing situ hybridization to detect mRNA in the fish embryo.

50. The method of claim 45, wherein the assay comprises staining with 25 a labelled antibody to detect a protein in the fish embryo.

51. The method of claim 45, wherein the cancerous cells are labelled with a marker.

30 52. The method of claim 51, wherein the marker is a fluorescent marker.

53. The method of claim 7, further comprising formulating the agent with a pharmaceutically acceptable carrier as a pharmaceutical composition.

5 54. A method of screening an agent for activity against cancerous cells, comprising

introducing one or more cancerous cells into a population of fish ;
administering the agent to the population of fish; and
monitoring an effect of the agent on development of the cancerous cells in the population of fish.

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55. The method of claim 54, wherein the monitoring comprises determining an EC50 for the effect of the agent on development of the cancerous cells in the fish.

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56. The method of claim 54, further comprising detecting an LD50 of the agent on the population of fish.

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57. The method of claim 54, wherein the method is repeated for a plurality of agents, and an agent with a low EC50|LD50 ratio is formulated with a carrier as a pharmaceutical composition.

58. The method of claim 54, wherein the fish is a zebrafish.

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59. A method of propagating cells, comprising introducing one or more heterologous cells into a fish; culturing the fish under conditions in which the cells proliferate; and recovering the proliferated cells.

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60. The method of claim 59, wherein the cells differentiate in the course of proliferation, and the cells are recovered as a differentiated tissue.

61. The method of claim 59, wherein the cells are stem cells.

62. The method of claim 59, wherein the cells are human cells.

63. The method of claim 59, further comprising introducing recovered cells into a patient.

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64. The method of claim 59, wherein the heterologous cells are obtained from the same patient into which recovered cells are transplanted.

10 65. The method of claim 59, wherein the heterologous cells are selected from the group consisting of osteoblast, osteoclast, chondrocytes, myocytes, neurons, pancreatic cells, hepatic cells glial cells, and renal cells.

66. A method of diagnosing a sample for a cancerous cell or pathogen, comprising:

15 obtaining a sample from a patient containing a population of cells; introducing the population of cells into a fish; detecting a property of the population of cells to indicate whether the population comprises a cancerous cell or pathogen.